In re Application of: Dror OFER
Serial No.: 10/523,131
Filed: January 21, 2005
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.
Group Art Unit: 1631
Attorney Docket: **35898**
Confirmation No.: 1264

In the Claims:

1. (Currently Amended) A method of obtaining information about a chemically active area of a target molecule, comprising:

(a) selecting a compound that is a substantially rigid chemical gauge comprising at least one set of three binding points in a substantially rigid triangular configuration, each of said at least one set of three binding points being selected capable of binding to a 3-point pharmacophore comprising a triplet of chemical binding points selected from the group consisting of acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor, and aromatic, wherein each pair of binding points of said 3-point pharmacophore is separated by a distance in a range of 2 to 12 angstrom;

(b) performing an assay for measuring an interaction of said target molecule with said gauge, thereby obtaining an assay result for said gauge;

(c) selecting additional substantially rigid chemical gauges according to said (a) so as to obtain a plurality of gauges, such that for a portion of triangle space comprising 50 % of said triangle space, said plurality of gauges is selected such that for each 3-point pharmacophore corresponding to a point in said portion of triangle space, said plurality of gauges comprises~~so as to comprise~~ at least six gauges with a substantially rigid triangular configuration of binding points capable of chemically binding to said~~each~~ 3-point pharmacophore~~ corresponding to a point in said portion of triangle space~~, wherein said triangle space defines all possible 3-point pharmacophores defined by a triplet of distances that form a triangle, each distance being in a range of 2-12 angstrom, and by a triplet of chemical binding point types for the triangle vertices, each chemical binding point type being selected from the group consisting of acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor, and aromatic, and wherein said point in said triangle space is defined by six coordinates, three of said coordinates being for defining the three distances in said

In re Application of: Dror OFER
Serial No.: 10/523,131
Filed: January 21, 2005
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.
Group Art Unit: 1631
Attorney Docket: **35898**
Confirmation No.: 1264

triplet of distances, and three of said coordinates being for defining the three binding point types in said triplet of chemical binding point types;

(d) performing said (b) for each of said additional substantially rigid chemical gauges, so as to obtain a plurality of assay results; and

(e) identifying a plurality of spatially and chemically specific configurations of binding points in said chemically active area of said target molecule using a computational model in which said assay results represent interactions between configurations of binding points in said chemically active area and triangular geometric substructures, each triangular geometric substructure representing a set of three binding points of a gauge and being defined by a triplet of distances that form a triangle and by a triplet of chemical binding point types for the triangle vertices,

thereby obtaining information about said chemically active area.

2. (Previously Presented) A method according to claim 1, wherein said additional gauges are selected such that for a portion of triangle space comprising 50 % of a triangle space that defines all possible 3-point pharmacophores defined by a triplet of distances that form a triangle, each distance being in a range of 4-8 angstrom, and by a triplet of chemical binding point types for the triangle vertices, each chemical binding point type being selected from the group consisting of acid, base, hydrophobic, hydrogen-bond donor, hydrogen-bond acceptor, and aromatic, said plurality of gauges is selected so as to comprise at least six gauges with a substantially rigid triangular configuration of binding points capable of chemically binding to each 3-point pharmacophore corresponding to a point in said portion of triangle space.

3. (Original) A method according to claim 1, wherein said gauges are constructed using a rigid scaffold.

In re Application of: Dror OFER
Serial No.: 10/523,131
Filed: January 21, 2005
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.
Group Art Unit: 1631
Attorney Docket: **35898**
Confirmation No.: 1264

4. (Original) A method according to claim 1, wherein constituent atoms of said gauges do not move more than 1 Å unless at least 20Kcal/Mol are applied to the gauge.

5. (Canceled)

6. (Previously Presented) A method according to claim 1, wherein said spatially and chemically specific configurations comprise 3-point pharmacophores.

7. (Withdrawn) A method according to claim 1, wherein identifying comprises identifying a 3-point pharmacophore that matches a triangular configuration of a bound gauge.

8. (Previously Presented) A method according to claim 1, wherein identifying comprises identifying a 3-point pharmacophore that does not match a triangular configuration of a bound gauge.

9. (Original) A method according to claim 8, wherein identifying comprises identifying by statistical analysis of said assay results.

10. (Withdrawn) A method according to claim 9, wherein identifying comprises identifying by clustering.

11. (Withdrawn) A method according to claim 1, wherein identifying comprises assuming each gauge indicates a single configuration.

12. (Withdrawn) A method according to claim 1, wherein identifying comprises assuming at least some of the gauges indicate a plurality of configurations.

13. (Withdrawn) A method according to claim 1, wherein identifying comprises classifying gauges by chemical moieties at vertexes of said configurations.

14. (Previously Presented) A method according to claim 1, comprising reconstructing a spatial map of at least part of said chemically active area, from at least two of said assay results, said spatial map including at least four chemical binding areas.

15. (Previously Presented) A method according to claim 14, wherein said spatial map includes at least six chemical binding areas.

16. (Withdrawn) A method according to claim 1, comprising reconstructing a spatial map of at least part of said chemically active area, from at least two of said configurations, said spatial map including at least four chemical binding points.

17. (Withdrawn) A method according to claim 16, wherein said spatial map includes at least six chemical binding areas.

18. (Withdrawn) A method according to claim 16, wherein reconstructing comprises:

test-reconstructing a plurality of spatial maps from said configurations;
scoring said maps; and
selected a spatial map based on its score.

19. (Withdrawn) A method according to claim 16, wherein reconstructing comprises:

test-reconstructing a plurality of spatial maps from said configurations;

clustering said maps according to common substructures; and

selected a spatial map based on a relative property of a cluster it belongs to.

20. (Withdrawn) A method according to claim 19, wherein said relative property comprises size.

21. (Original) A method according to claim 16, wherein said spatial map includes enough binding points to ensure binding of a small molecule drug having a chemical profile matching the binding points.

22. (Withdrawn) A method according to claim 21, wherein said spatial map includes at least 6 binding points.

23. (Withdrawn) A method according to claim 21, wherein said spatial map includes at least 8 binding points.

24. (Previously Presented) A method according to claim 1, wherein said plurality of gauges comprises a set of gauges with at least 10,000 distinct gauges.

25. (Previously Presented) A method according to claim 1, wherein said plurality of gauges comprises a set of gauges with at least 50,000 distinct gauges.

26-28. (Canceled)

29. (Previously Presented) A method according to claim 1, wherein at least 0.5% of said gauges bind with said target when said target is interacted with said gauges.

30. (Previously Presented) A method according to claim 1, wherein at least 1% of said gauges bind with said target when said target is interacted with said gauges.

31. (Previously Presented) A method according to claim 1, wherein at least 3% of said gauges bind with said target when said target is interacted with said gauges.

32. (Original) A method according to claim 1, wherein at least 50% of said gauges are defined by adding moieties to a set of fewer than 100 scaffolds.

33. (Original) A method according to claim 1, wherein at least 50% of said gauges are defined by adding moieties to a set of fewer than 50 scaffolds.

34. (Previously Presented) A method according to claim 1, wherein said plurality of gauges uses fewer than 15 different chemical moieties to define the chemical behavior of said gauges.

35. (Previously Presented) A method according to claim 1, wherein said plurality of gauges uses fewer than 10 different chemical moieties to define the chemical behavior of said gauges.

36. (Original) A method according to claim 1, wherein said assay is a functional assay.

37. (Withdrawn) A method according to claim 1, wherein said assay is a binding assay.

38. (Withdrawn) A method according to claim 1, wherein said assay is a cellular assay.

39. (Withdrawn) A method according to claim 1, wherein said assay is a flow-through assay.

40. (Original) A method according to claim 36, wherein said functional assay is performed in the presence of a natural substrate of said target.

41. (Original) A method according to claim 1, wherein said target comprises a protein including a biochemically active area adapted to engage a substrate.

42. (Original) A method according to claim 41, wherein said chemically active area comprises an area including said biochemically active area.

43. (Original) A method according to claim 41, wherein said chemically active area comprises a control area of said protein.

44. (Previously Presented) A method according to claim 1, wherein said plurality of assay results comprises assay results showing successful binding of at least 60 distinct gauges.

45. (Previously Presented) A method according to claim 1, wherein said plurality of assay results comprises assay results showing successful binding of at least 10 distinct gauges.

46. (Previously Presented) A method according to claim 1, wherein said plurality of assay results comprises assay results showing successful binding of at least 100 distinct gauges.

47. (Previously Presented) A method according to claim 1, wherein identifying comprises identifying at least 40 different configurations.

48. (Previously Presented) A method according to claim 1, wherein identifying comprises identifying at least 10 different configurations.

49. (Previously Presented) A method according to claim 1, wherein identifying comprises identifying at least 100 different configurations.

50. (Withdrawn) A method according to claim 16, comprising:

comparing said map to a lead data base; and

selecting a lead from said data base for further use responsive to a semblance or lack of semblance between said lead and said map.

51. (Withdrawn) A method according to claim 16, comprising:

comparing said map to a lead data base; and

rejecting a lead from said data base for further use responsive to a semblance between said lead and said map.

52. (Withdrawn) A method according to claim 16, comprising:

constructing a lead to have a semblance to said map.

53. (Withdrawn) A method according to claim 52, wherein constructing comprises constructing using said gauges or scaffolds used to define said gauges.

54. (Previously Presented) A method according to claim 1, comprising:

comparing said configurations to a lead data base; and

selecting a lead from said data base for further use responsive to a matching of said configurations to said lead.

55. (Previously Presented) A method according to claim 1, comprising:

constructing a lead based on said configurations.

56. (Previously Presented) A method according to claim 1, comprising:

selecting at least one of said gauges as a lead for drug discovery.

57. (Withdrawn) A method according to claim 1, comprising comparing the binding of gauges with similar binding geometries to obtain steric clashing data; and

analyzing said steric clashing data to provide geometrical information about said target.

58–101. (Cancelled)

102. (Withdrawn) A method according to claim 1, comprising generating a set of drug leads for said target based on said information.

In re Application of: Dror OFER
Serial No.: 10/523,131
Filed: January 21, 2005
Office Action Mailing Date: September 2, 2010

Examiner: Borin, Michael L.
Group Art Unit: 1631
Attorney Docket: **35898**
Confirmation No.: 1264

103. (Withdrawn) A method according to claim 102, comprising removing known drug leads for said target from said set.

104–156. (Cancelled)

157. (Withdrawn) A method according to claim 1, wherein said identifying comprises taking said rigidity into account in said model.

158. (Previously Presented) A method according to claim 1, wherein said target molecule comprises an agricultural chemical target.

159. (Previously Presented) A method according to claim 1, wherein said target molecule comprise a drug target.

160. (Canceled)

161. (Previously Presented) A method according to claim 1, wherein at least 0.1% of said gauges bind with said target when said target is interacted with said gauges.

162. (Previously Presented) A method according to claim 1, wherein said binding points of said gauges comprise Hydroxyl (OH), Carboxyl (COOH), Amide (CONH2), Ethyl (CH2-CH3), Propyl (CH2-CH2-CH3), Phenyl (C6H5, 6 member aromatic ring).

163. (Previously Presented) A method according to claim 1, wherein said chemically active area comprises at least two disjoint chemically active areas.

164-171. (Cancelled)